

**ABSTRACT OF THE DISCLOSURE**

There are many situations where oligonucleotides that efficiently bind a target DNA or RNA are desired. These oligonucleotides can be used for a variety of purposes, including antisense, diagnostics, and array generation. While researchers have worked for many years to identify algorithms and methods for predicting the oligonucleotides that will bind the target with the highest efficiency, better prediction methods are needed. Disclosed are methods, articles, machines, and compositions that aid in identifying oligonucleotides and sets of oligonucleotides that will efficiently bind a target nucleic acid molecule. Also disclosed are optimized sets of oligonucleotides that bind HIV-1 genomic RNA or DNA, such as the GAG RNA, and methods of using them.